FUNCTIONAL DELINEATION OF PREFRONTAL NETWORKS UNDERLYING WORKING MEMORY IN SCHIZOPHRENIA: A CROSS-DATASET EXAMINATION

Research objectives:
Working memory (WM) impairment in schizophrenia substantially impacts functional outcome. Although the dorsolateral prefrontal cortex (dlPFC) has been implicated in such impairment, a more comprehensive examination of brain networks comprising PFC is warranted. The present research used a whole-brain, multi-experiment analysis to delineate task-related networks comprising PFC. Activity was examined in schizophrenia patients across a variety of cognitive demands.

Methods:
100 schizophrenia patients and 102 healthy controls completed one of four fMRI tasks: a verbal WM task, a visuospatial WM task, a set-switching task, and a thought generation task. Task-related networks were identified using multi-experiment constrained principal component analysis for fMRI (fMRI-CPCA). Effects of task conditions and group differences were examined using mixed-model analysis of variance on the task-related activity. Correlations between task performance and brain activity were also examined.

Results:
Four spatially and temporally distinct networks with PFC activation emerged, and were postulated to subserve: (1) internal attention, (2) auditory-motor attention, (3) motor responses, and (4) task energizing. The “energizing” network – engaged during WM encoding, and diminished in patients – was correlated with accuracy in the verbal and visuospatial WM tasks, and with WM capacity measured out-of-scanner. The dlPFC-dominated “internal attention” network exhibited hypoactivity in patients, but was not correlated with WM performance.

Conclusions:
Multi-experiment analysis allowed delineation of PFC-anchored networks across different cognitive constructs. The results suggest that WM deficits in schizophrenia arise from disruption in early task-energization processes. While there was some evidence for disruption in the dlPFC network, such dysfunction may not underlie WM capacity.